retropalateal and pharyngeal airways. Lateral pharyngeal fat pad is immediately lateral to the muscles that form the lateral wall of the fat pad. The lateral pharyngeal fat pad is immediately tissue pressure in one location, the lateral pharyngeal did it change with breathing? We chose to measure pressures, did it change with breathing and, if so, how and pharyngeal pressures. If it did differ from these the pressure in the tissue differed from atmospheric pressure, however, the pressure in tissues surrounding the pharyngeal airway (3). The airway (9), on the pressure within the airway, and on that it would be determined by a number of influences, would not always be equal to atmospheric pressure and masked and pharyngeal pressure with a balloon catheter. Pfp differed from atmospheric pressure, generally exceeding it, and from pharyngeal pressure. Pfp correlated positively with airflow and with pharyngeal pressure, decreasing during inspiration and increasing during expiration. Changes in Pfp with ventilation were eliminated by oropharyngeal intuba- tion. We conclude that Pfp differs from atmospheric and pharyngeal pressures and that it changes with breathing. pharyngeal airway; upper airway; fat; sleep apnea syndromes

THE SIZE AND SHAPE of the pharyngeal airway are thought to depend on the balance of forces (1, 6) developed by muscles that contract to expand the airway (9), on the pressure within the airway, and on the pressure in tissues surrounding the airway (3). The pressure in tissues surrounding the airway, however, has never been measured to our knowledge. Isono and Remmers (3) postulated, however, that this pressure would not always be equal to atmospheric pressure and that it would be determined by a number of influences, some of which operate at a considerable distance from the pharyngeal lumen.

The purpose of this study was to attempt to measure the pressure in tissue surrounding the pharyngeal airway. We specifically wished to determine whether the pressure in the tissue differed from atmospheric and pharyngeal pressures. If it did differ from these pressures, did it change with breathing and, if so, how did it change with breathing? We chose to measure tissue pressure in one location, the lateral pharyngeal fat pad. The lateral pharyngeal fat pad is immediately lateral to the muscles that form the lateral wall of the retropalataline and pharyngeal airways.

METHODS

Subjects. Six male pigs with a wide range of age, 3–40 mo, and a similar large range of weight, 29–140 kg, were used (Table 1). We chose these large ranges to determine whether the tissue pressure changes we would observe would be age and weight dependent. Pigs 1 and 2 were Yucatan micro pigs, whereas pigs 3–6 were Yorkshire pigs. The pigs were housed in the University of Virginia's Medical Research Building. All of the subjects were observed to be healthy before and during their studies, and all animal procedures were reviewed and approved by the Animal Research Committee.

Placement of pressure transducer in fat pad. Pigs were initially given an intramuscular injection of tiletamin and zolazepam (6 mg/kg) and xylazine (2 mg/kg). A 1½-in. 20-gauge intravenous catheter was placed in an ear vein and attached to an intermittent injection cap. At ~1-h intervals they were given intramuscular injections of tiletamin and zolazepam (1.5 mg/kg) and xylazine (0.5 mg/kg) to maintain anesthesia. The pigs were placed supine in the gantry of a computed tomographic (CT) scanner (model PQ, 2000, Picker, Cleveland, OH). Head position was kept constant by aligning x- and y-coordinate marks drawn on the head with the x and y laser lights projected from the CT scanner onto the head. A lateral scout image was obtained, followed by axial images at 5-mm intervals of the upper airway; axial images were obtained with a 25° cephalad tilt. The skin medial and ventral to the mandible was anesthetized with 2% lidocaine. A Seldinger needle (18 gauge, 2½ in. long, thin wall) was inserted into the lateral pharyngeal fat pad, and its position within the fat pad was verified by CT scans. Axial images were periodically repeated during the procedure to verify instrument position.

A guide wire (0.038 in. diameter, 100 cm long, 3-mm curve radius; Cook, Bloomington, IN) was inserted through the needle; the needle was then removed, leaving the tip of the guide wire in place in the lateral pharyngeal fat pad. Dilator catheters, 8- and then 10-Fr, were placed in succession over the guide wire followed by a peel-away sheath (11-Fr, 15 cm long, Medi-Tech, Watertown, MA). A Millar catheter with a transducer on its tip (model SPC-350, Millar Instruments, Houston, TX) was then inserted through the sheath into the lateral pharyngeal fat pad. The peel-away sheath was then removed, and the position of the transducer tip catheter was confirmed by using CT scans.

To determine how catheter position influenced results, in pig 6, after studies were completed on the right fat pad, the catheter was forcibly pushed into the fat pad and the studies were repeated. Then the catheter was withdrawn from the right fat pad and placed in the left fat pad. Measurements were made, the catheter was then withdrawn incrementally, and measurements were repeated at each location.

Pressure and flow measurements. Tissue pressure was recorded from the transducer-tipped catheter. Pharyngeal pressure was measured with a 1-cm-long Hyatt-type balloon (A&E Medical, Farmingdale, NJ) and with no. 100 polyethylene tubing that had multiple holes in the distal portion, which was covered by the balloon. The balloon was inserted through the mouth, placed caudal to the soft palate, and inflated with 0.25 ml of air. The tubing was attached to a differential pressure transducer (model MP 45-28-871, Vali- dyne Engineering, Northridge, CA). The other port of the transducer was attached to a face mask with a rubber seal that was placed over the nose and mouth.
A Fleisch pneumotachograph was attached to the face mask to measure airflow. The ports of the pneumotachograph were attached to a pressure transducer (2 cmH₂O; model MP 45-14-871, Validyne Engineering), and flow was calibrated to 1 l/s by using a rotometer. The face mask was a large clear lexan conical canine mask (Webster, Sterling, MA). It was 4 ¾ in. long and was covered at the large end of the cone with a highly flexible rubber diaphragm with an outer diameter of 5 ½ in. and a 2 ½-in. hole in the middle. The pig’s nose and mouth were placed in the hole of the diaphragm, and the mask was advanced over the snout until there was no apparent air leak. The diaphragm restricted but did not prevent the pig from opening its mouth. We did not control or monitor whether the pig breathed through its nose or mouth.

Signal processing. Data were recorded on a portable computer (Dolch V-P.A.C 386, San Jose, CA) utilizing AT/MCA-CODAS hardware and software (DATAQ Instruments, Akron, OH) at 40 Hz. Signals were displayed during the study for calibration and for reference.

Protocol. After the transducer-tipped catheter was inserted, the pig was allowed to breathe spontaneously while we measured tissue pressure, pharyngeal pressure, and flow. In four pigs (1–3 and 5), after measurements were obtained, an endotracheal tube was inserted through the mouth into the trachea, the cuff was inflated, and the pneumotachometer was attached to endotracheal tube. Measurements of tissue pressure, pharyngeal pressure, and flow were repeated. In two animals, a fixed inspiratory resistance (42 cmH₂O·l⁻¹·s⁻¹) was added to the endotracheal tube to simulate and exceed the higher resistance that occurred when the animals breathed through their nose and mouth.

Data analysis. All signals were imported into a spreadsheet (Excel, Microsoft, Redmond, WA) for comparisons and for statistical analysis.

Transmural pressure (Ptm) was calculated by subtracting fat pad pressure (Pfp) from pharyngeal pressure (Pph) (Ptm = Pph – Pfp). Transmural pressure was plotted against flow, and linear regression analysis was performed on the entire curve, on the inspiratory limb and then on the expiratory limb of the curve. To look for hysteresis in the transmural pressure-flow relationship, we selected data points from both late expiration and early inspiration and then from both late inspiration and early expiration. We then calculated the slopes of the lines formed by each set of data points and the intercepts of transmural pressure at zero flow by using linear regression analysis. Transmural pressure at end inspiration was taken as the zero-flow intercept of the curve consisting of data points from late inspiration and early expiration. Transmural pressure at end expiration was taken as the zero-flow intercept of the curve consisting of data points from late expiration and early inspiration. Transmural pressures at end inspiration were compared with transmural pressures at end expiration with a paired t-test. We also examined separately the transmural pressure-flow relationship for early inspiration, for late inspiration, for early expiration, and for late expiration by using linear regression analysis. Other data were also analyzed with univariate regression analysis.

![Computerized tomographic scan showing transducer-tipped catheter in fat pad space. Retropalatal airway is elliptical-like black space to left of catheter tip, soft palate is above retropalatal airway, and oral airway is triangular-like black space above soft palate.](image)
RESULTS

Pressure was measured in the fat pad at a distance of 1.1–2.0 cm lateral to the airway (Fig. 1).

In all animals, pressure in the fat pad was higher during expiration than during inspiration. There was a significant positive linear correlation between airflow and pressure in the fat pad in each animal (Fig. 2A). The slopes of the linear regression equations for the pressure-flow curves (pressure on x-axis, flow on y-axis) were always positive and ranged from 0.081 to 0.18 l·s\(^{-1}\)·cmH\(_2\)O\(^{-1}\) [mean 0.12 ± 0.044 (SD) l·s\(^{-1}\)·cmH\(_2\)O\(^{-1}\)].

Pressure in the fat pad exceeded atmospheric pressure at all times in three pigs (1, 2, and 4) and most of the time in three pigs (3, 5, and 6) (Fig. 2A). The maximal pressure recorded was 24 cmH\(_2\)O, and the minimal was −3 cmH\(_2\)O. Pressure in the fat pad was independent of the age and weight of the pigs.

Pressure in the fat pad also correlated linearly with pharyngeal pressure in all animals (Fig. 2B). Increases in fat pad pressure were associated with increases in pharyngeal pressure while decreases in fat pad pressure were associated with decreases in pharyngeal pressure. The slope of the curve (fat pad pressure on the

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Fig. 2. A: fat pad pressure correlated with flow in all pigs. B: fat pad pressure correlated with pharyngeal pressure in all pigs.
x-axis, pharyngeal pressure on the y-axis) was >1 in all pigs except pig 4 (slope in pig 4 = 0.85).

Orotracheal intubation markedly decreased the changes in fat pad pressure during breathing (Fig. 3). This was reflected by a significant increase in the slope of the pressure-flow curve in three of the four animals that were intubated and by the absence of any significant relationship between flow and fat pad pressure in the fourth. The addition of an inspiratory resistance to the orotracheal tube did not significantly change fat pad pressure from the values during intubation without the inspiratory resistance.

The variability of fat pad pressure when the catheter was forced in, placed in the contralateral fat pad, and then incrementally withdrawn is shown in Fig. 4. Forcing the catheter in the fat pad increased the pressure at all flows and decreased the slope (Fig. 4A, bottom). Fat pad pressure measured in the contralateral left fat pad (Fig. 4B) continued to increase with expiration and decrease with inspiration, but the slope and intercept of the curves were lower than on the right side. When the catheter was withdrawn 2.8 cm from the lateral edge of the retropalateal airway, the catheter detected smaller changes in tissue pressure than when it was closer to the airway.

Transmural pressure and flow during breathing are shown in Fig. 5. The slopes of the line derived from both inspiration and expiration were positive in all pigs except that in pig 4 the relationship was not significant because the line was vertical. Separation of inspiration from expiration revealed that the slope of the line derived from inspiration alone was positive in all pigs except pig 4. The slope of the line derived from expiration alone was also positive in all pigs except pig 5. The slope of the expiration portion of the curve was greater than the inspiration portion in all pigs except pig 6.

Further analysis of the transmural pressure-flow relationship was performed by combining late inspiration with early expiration and then combining late expiration with early inspiration. The slopes of these lines were always positive and not significantly different from one another in each pig. In pig 4, however, the slope of late expiration and early inspiration was not significant so that in this pig no comparison could be made between the two phases of ventilation. The zero-flow intercept of these lines revealed that transmural pressure at end expiration (calculated from the late expiration-early inspiration curve) was higher than transmural pressure at end inspiration (calculated from the late inspiration-early expiration curve) in all five pigs in which significant zero-flow intercepts could be calculated (P < 0.02; Table 2).

Transmural pressures relative to flow in early inspiration, late inspiration, early expiration, and late expiration are shown in Fig. 6. The slopes of the regression lines for each of these ventilatory phases are shown in Table 3. Many slopes were not significant, and no consistent differences among the different ventilatory phases were apparent.

Fig. 3. Orotracheal intubation markedly decreased changes in fat pad pressure during breathing in the 4 pigs that were intubated.

Fig. 4. Fat pad (FP) pressure in right fat pad (A) and left fat pad (B). Distance from tip of catheter to lateral edge of retropalateal airway is shown in cm on each graph.
DISCUSSION

This study has shown that pressure in the lateral pharyngeal fat pad is different from both atmospheric and pharyngeal pressures. Fat pad pressure generally exceeded atmospheric pressure. Fat pad pressure was positively correlated with pharyngeal pressure and varied with breathing. During expiration, fat pad pressure increased, and during inspiration it decreased. Orotracheal intubation eliminated most of these changes in fat pad pressure during breathing.

This study thus confirms the predictions of Isono and Remmers (3) that the pressure in tissues surrounding the upper airway differs from atmospheric pressure. This study also reveals that the pressure in the lateral pharyngeal fat pad is closely linked to breathing. This initial study of tissue pressure does not, however, reveal what influences fat pad pressure and how it is linked to breathing. Also, because we did not measure the force of muscles acting on the upper airway, this study is not able to confirm the balance of forces theory.

The close linkage between fat pad and pharyngeal pressures may be simply due to transmission of pharyngeal pressure through the lateral pharyngeal wall into the fat pad. This mechanism is suggested by elimination of changes in fat pad pressure with intubation.

Another possible mechanism linking changes in fat pad pressure to breathing is via tracheal tug. Caudal movement of the trachea in dogs has been shown to decrease upper airway resistance (8); this occurs through caudal traction on cervical structures mechanically linking the thorax and the upper airway. The precise mechanism of how and where tracheal tug expands the upper airway is unknown. Caudal traction on these structures could also tug on the fat pad and decrease its pressure. In the present study we anchored the trachea by intubating it and preventing it from moving caudally during inspiration. Thus we cannot exclude tracheal tug as a mechanism of changing fat pad pressure during breathing. Studies with isolated laryngeal and thoracic trachea will be necessary to test whether tracheal tug influences fat pad pressure. These studies could also determine whether changes in pharyngeal pressure are transmitted directly to the fat pad.

Fat pad pressure might also be altered by contraction of upper airway muscles. These muscles could be either adjacent to the fat pad or attached to other structures that are adjacent to the fat pad. We know of no muscles, however, with respiratory activity that are adjacent to the fat pad that might increase fat pad pressure during expiration and decrease it during inspiration.

Because the density of fat (0.9 gm/cm³) is less than that of water, the major component of most tissues, fat is more compressible than most tissues. When fat is surrounded by more rigid tissues, it could act as a hydraulic to transfer pressures generated in one location to another location. For example, caudal traction

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Fig. 5. Transmural pressure and flow during breathing. Regression equations are shown for expiration, inspiration, and both inspiration and expiration (Ins & Exp) on each graph.
on the inferior portion of the fat pad would lower the pressure throughout the entire fat pad just as lowering pressure at the valve stem of a tire lowers pressure throughout the tire. If there were a very compliant structure adjacent to the fat pad such as the lateral pharyngeal wall, the lateral pharyngeal wall would be pulled into the fat pad space and enlarge the upper airway. This mechanism can be tested in future studies. Because the physical characteristics of fat in the lateral pharyngeal fat pad are unknown, it would also be important in future studies to determine the density and connective tissue structure of fat in this location.

The close correlation between fat pad and pharyngeal pressures suggests that the fat pad could act as a spring to absorb and return forces created by changes in pharyngeal pressure. When pharyngeal pressure increases during early expiration, the lateral pharyngeal wall moves laterally (7). This would be expected to compress and increase the pressure in the fat pad. When pharyngeal pressure returns to atmospheric pressure such as at the end of expiration, the fat pad would return the pressure to the lateral airway wall and narrow the airway. During inspiration, when pharyngeal pressure decreased, the higher pressure in the fat pad would be expected to press the lateral pharyngeal airway wall into the pharynx unless fat pad pressure fell more than pharyngeal pressure or unless the lateral pharyngeal wall stiffened because of muscle contraction or passive lengthening. During sleep when muscle tone decreases, the airway would be more susceptible to narrowing caused by fat pad pressure on the lateral pharyngeal wall.

As mentioned above, during inspiration when pharyngeal pressure decreases, the fat pad would be expected

<table>
<thead>
<tr>
<th>Pig No.</th>
<th>Transmural Pressure, cmH2O</th>
<th>End inspiration</th>
<th>End expiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>−8.7</td>
<td>−8.5</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>−27.3</td>
<td>−17.5</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2.77</td>
<td>−1.1</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>−11.0</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>−7.43</td>
<td>−1.99</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>−13.2</td>
<td>−10.6</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Transmural pressure at zero flow at end inspiration and at end expiration

<table>
<thead>
<tr>
<th>Pig No.</th>
<th>Slope Early inspiration</th>
<th>Late inspiration</th>
<th>Slope Early expiration</th>
<th>Late expiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.014</td>
<td>0.0069</td>
<td>NS</td>
<td>0.026</td>
</tr>
<tr>
<td>2</td>
<td>NS</td>
<td>0.0019</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>3</td>
<td>0.019</td>
<td>0.027</td>
<td>NS</td>
<td>0.014</td>
</tr>
<tr>
<td>4</td>
<td>−0.067</td>
<td>NS</td>
<td>NS</td>
<td>0.024</td>
</tr>
<tr>
<td>5</td>
<td>0.025</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>6</td>
<td>0.012</td>
<td>0.010</td>
<td>0.012</td>
<td>0.1</td>
</tr>
</tbody>
</table>

NS, not significant.

Table 3. Slopes of transmural pressure-flow relationship as shown in Fig. 6

Fig. 6. Transmural pressure and flow during breathing for early inspiration (●), late inspiration (○), early expiration (●), and late expiration (○). Points for late inspiration and early expiration were combined to calculate transmural pressure at zero flow for end inspiration. Similarly, points for late expiration and early inspiration were combined to calculate transmural pressure at zero flow for end expiration. See Tables 2 and 3 for statistical analysis.
to press on the lateral pharyngeal wall and narrow the airway unless fat pad pressure fell more than pharyngeal pressure or the lateral pharyngeal wall stiffened. In our anesthetized pigs, pharyngeal pressure changes exceeded the changes in fat pad pressure in five of six animals. This suggests that in these animals during inspiration, pharyngeal pressure would fall more than fat pad pressure and the upper airway would be vulnerable to compression from the fat pad unless the lateral pharyngeal wall stiffened.

The muscles that comprise most of the lateral pharyngeal wall are the superior and possibly the middle pharyngeal constrictors. Contraction of these muscles would probably stiffen the muscles and diminish transmission of pressure to the fat pad. In normal humans, Kuna (4) found that phasic activation of these muscles with breathing occurred only occasionally in awake subjects, sporadically in rapid-eye-movement sleep, and not at all during non-rapid-eye-movement sleep (4). In decerebrate tracheotomized cats, however, these muscles contracted when the airway was small, tending to enlarge it (5). It is possible that the anesthesia in our pigs decreased contraction of the lateral constrictors more than occurs during sleep and thus augmented the transmission of pressure from the pharynx to the fat pad.

If the fat content of fat pad cells increases with weight gain, either the pressure within the fat pad would increase or the fat pad would increase in size and displace more compliant adjacent structures. This could displace the lateral pharyngeal wall into the upper airway if the lateral pharyngeal wall muscles are not contracting or are not stiffened by being stretched. We recently demonstrated that increasing the volume of the fat pad space did narrow the upper airway of anesthetized pigs (10). This suggests that an increase in the fat content of fat cells could narrow the upper airway.

Measurement of fat pad pressure allowed us to calculate airway transmural pressure. Transmural pressure (Ptm = Pph − Pfp) represents the dilating and compressing forces on the airway. An increase in transmural pressure implies airway dilatation, whereas a decrease in transmural pressure suggests airway compression (3). During inspiration, transmural pressure decreased in the five of six pigs, as reflected by a positive slope indicating that both transmural pressure and flow were decreasing together. During expiration both transmural pressure and flow increased in five of six pigs, as again reflected by a positive slope. These data suggest that the airway was compressed during inspiration in five pigs and dilated in expiration in five pigs. Although we found the slopes to be greater in expiration than in inspiration in five of six pigs, the low correlation coefficients of some of the curves make comparison of small differences in slopes questionable.

Our data suggest there may be hysteresis in the transmural-flow pressure relationship. Transmural pressure at end expiration was higher than at end inspiration in five pigs in which it could be detected. When intraluminal pressure is zero, any differences in transmural pressure can be attributed to differences in fat pad pressure. Thus the lower transmural pressure at end inspiration suggests more airway compression due to fat pad pressure than at end expiration.

There are several inherent technical difficulties in measuring tissue pressure that may influence measurements of fat pad pressure. First, introduction of a catheter into a previously intact tissue may compress the tissue lateral to the transducer and thus increase pressure measured by the transducer. We did observe that forcing an already placed catheter in further did increase measured pressure. Second, local surface forces between tissue-sensor contract points may induce artifacts in the measurements. Both of these reasons may explain the difference we observed between catheter pressure observed in the left and right fat pads of the same pig. Despite these problems and limitations, however, we did observe consistent changes in fat pad pressure during breathing.

CT scans show that both pigs and humans (2) have fat pads lateral and adjacent to their upper airway muscles. This suggests that our data obtained by using the fat pad and upper airway of pigs may be applicable to humans.

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